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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,091	05/06/2005	Juha-Matti Savola	TUR-168	2654

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
05/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,091	SAVOLA ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 25-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23 and 25-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/17/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/17/09 has been entered.

2. Applicant's arguments filed 2/17/09 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 23 and 26-33 are pending in this office action. Claim 33 is newly added.

5. Claim 23 is objected to because of the following informalities: the word substantially is mistyped; y is missing at the end. Appropriate correction is required.

6. The information disclosure statement (IDS) submitted on 2/17/09 is acknowledged and has been reviewed.

7. The rejection of claims 23-32 under 35 U.S.C. 103(a) as being unpatentable over Karjalainen et al. (US 5,498,623) in view of Geerts et al. (US 5,658,938) and further in view of Chauveaux et al. (US 6,326,401) and Huupponen et al. (1995) and Smith et al., (US 2004/0236108) is withdrawn in view of the rejection below.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

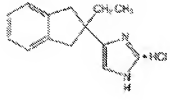
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

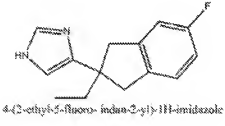
Claims 23 and 26-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

No proper antecedent basis or conception in context with that described within the specification is apparent for the phrase "of all or substantially all of the active ingredient" as recited in the instant claim 23; thereby constituting New Matter.

Affidavit

9. The affidavit under 37 CFR 1.132 filed on 2/17/09 by Juha-Matti Savola is persuasive with regards the data on the QT. However the declaration is not persuasive to overcome the rejection of claims 23 and 26-33 under 103 based on Huupponen

because Huupponen specifically teaches an α_2 adrenergic receptor antagonist (i.e., atipamezole) that has the same unexpected results when administered oramucosally. In summary Huupponen teaches the same ranges employed with the drug femiprazole (i.e., 5 and 10 mg in a spray) in dogs (see page 507 under subheading Drug administration). Huupponen teaches that of atipamezole administered via oromucosally had an increased bioavailability of about 33% and a more uniform absorption (see page 510 under Discussion) versus a "very poor" plasma bioavailability after oral dosing. Also Huupponen teaches that the oromucosal administration does not affect plasma epinephrine or norepinephrine concentrations, blood pressure or heart rate. Please note that atipamezole (i.e., 

) is very similar to 

), and therefore, it is reasonable to have the same unexpected results as taught by Huupponen.

The declaration/affidavit has been fully considered fail to be persuasive as discussed above and rejected below.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

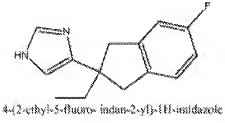
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 25-29 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huupponen (1995) in view of Karjalainen et al., (US 5,498,623).

Huupponen teaches an α_2 adrenergic receptor antagonist (a species of the generic formula I in its acid salt) that is administered in the form of a spray oromucosally

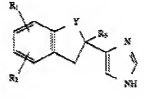
(see page 506, abstract; and Introduction as required by instant claim 23 in part, dissolved in ethanol and water (i.e., solvent; as required by instant claims 26- 27 in the form of spray as required by instant claims 31 and 32.

However Huupponen fails to teach the exact compound

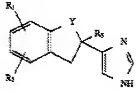


4-(2-ethyl-5-fluoro- indan-2-yl)-1H-imidazole as required by instant claims 23 and 35 in part, and also fails to teach the formulation consists of a preservative (i.e., methyl parahydroxybenzoate) and the flavoring agent aspartame and black currant as in claims 29-30 and 33, and also the addition of a preservative and a flavoring agent to the formulation (as required by instant claims 26, 28, 29).

Karjalainen et al. teach the claimed compound as in current claim



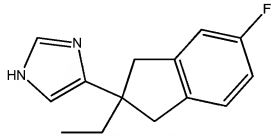
23 which is identical to the claimed compound of the claimed



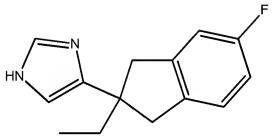
invention , wherein Y is CH_2 or CO, R_1 is a halogen or

hydroxyl, R_2 is hydrogen or halogen and R_3 is hydrogen or lower alkyl-methyl (see abstract in a pharmaceutical composition administered orally (see abstract and also see col. 4, lines 62-63). Reasonably to have an oromucosal administration.

With regards to claim 25 Karjalainen teaches (see abstract



also) 4-(2-ethyl-5-fluoro-2,3-dihydro 1H indan-2-yl)-1H-imidazole is the same as



4-(2-ethyl-5-fluoro- indan-2-yl)-1H-imidazole or its acid salts (i.e., hydrochloride salt of (see col. 7, lines 48-50).

Karjalainen et al. also teach that the solvent is ethanol (as required by instant claim 27; see col. 7, lines 63-64).

However Karjalainen fails to teach specifically oromucosal administration and the addition of a preservative and a flavoring agent to the formulation (as required by instant claims 26, 28, 29, 31-33). Even though Karjalainen failed to teach the addition of flavoring and or preservative it is however taught that "choosing auxiliary ingredients for the formulation is routine to the ordinary skill in the art and is evident that suitable solvents, colors etc are used in a normal way".

That being said it would have been obvious to one of ordinary skill in the art to add flavoring (i.e., sweetener) to the spray formulation for the improvement of the taste since the patient would preferably and willingly administer the sweet tasting spray versus a bitter tasting spay that is directly placed in the oromucosal cavity.
It would have been obvious to add a preservative to any drug formulation for the prolongation of shelf life. These are routine procedures employed in the art of formulation as indicated above by Karjalainen. One of ordinary skill in the art would have substituted Hupponen compound with Karjalainen since both compounds are α_2 adrenergic receptor antagonists and one would reasonably expect the formulation for oromucosal to be successful.

11. Claims 23, 25-30 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huupponen (1995) and Karjalainen et al., (US 5,498,623) in view of De Prost (US 6,413,988).

Huupponen and karjalainen are applied here as above. However both Huupponen and Karjalainen fail to teach the addition of a preservative and a flavoring agent to the formulation (as required by instant claims 26, 28, 29, 30 and 33).

De Prost teaches an aqueous pharmaceutical solution of prucalopride employed as a spray for oral administration that comprises a preservative for inhibiting the growth of micro-organism (see col. 2, lines 30-45 and col. 3, lines 14-16) wherein the preservative is a parahydroxybenzoate salt (see col. 4, lines 58-67) and the flavor is aspartame and black currant (see col. 2, lines 46-47 and col. 3, lines 1-4).

However De Prost fails to teach the claimed compound femiprazole and oromucosal administration.

It would have been obvious to one of ordinary skill in the art to have employed the teaching of De Prost of a spray formulation with a preservative and a sweetener with the teaching set forth by Huupponen and Karjalainen because as taught by De Prost these are added to liquid oral formulations such as sprays to inhibit microbial growth and to affect the taste by masking the bitter tasting effect. As known to one of ordinary skill in the art, aspartame is an intense sweetener and therefore capable of masking taste and black currant would give a fruity taste to the formulation and may enhance the sweetening capability of aspartame when combined.

Thus, the claimed invention was prima facie obvious to make and use at the time it was made

12. No claim is allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
4/23/09

/Robert C. Hayes/
Primary Examiner, Art Unit 1649